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EXAMINER	
LIU, SUE XU	

ART UNIT	PAPER NUMBER
1639	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/802,249	MAURITZ ET AL.	
	Examiner	Art Unit	
	Sue Liu	1639	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *02 October 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-13 and 15-26* is/are pending in the application.

4a) Of the above claim(s) *4-11 and 23-26* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-3, 12, 13 and 15-22* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claim Status

Claim 14 has been cancelled as filed on 10/2/07.

Claims 1-13 and 15-26 are currently pending.

Claims 4-11, and 23-26 have been withdrawn.

Claims 1-3, 12, 13 and 15-22 are being examined in this application.

Election/Restrictions

1. Applicant's election without traverse of Group I (Claims 1-22) in the reply filed on 10/18/06 is as previously acknowledged.

2. Applicant's election without traverse of the following species:

A.) nucleic acids for the biopolymers;

B.) fluorescent groups, specifically, stilbene, as the detectable protecting groups;

C.) Compound (f) in Figure 5 as the core structure;

in the reply filed on 10/18/06 and 3/6/07 is as previously acknowledged. Accordingly, Claims 4-11 are withdrawn due to non-elected species.

Priority

3. This application claims foreign priority to EPO 03006098.2 (3/19/03).

4. Receipt is acknowledged of papers submitted under 35 U.S.C. 119(a)-(d), which papers have been placed of record in the file.

Oath/Declaration

5. The new Oath/Declaration filed on 10/2/07 is acknowledged and entered.

Claim Rejections Withdrawn

6. In light of applicants' amendments to the claims canceling claim 15, amending Claim 19 to depend on claim 18 and amending claim 22, the following claim rejections as set forth in the previous office action are withdrawn:

Claims 15, 19 and 22 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

7. In light of applicants' amendment to the instant claim 1, the following claim rejection as set forth in the previous office action is withdrawn:

Claims 1-3, 12 and 13 are rejected under **35 U.S.C. 102(b)** as being anticipated by McGall et al (US 6,238,862; 05/29/2001).

Claim Rejections Maintained

Claim Rejections - 35 USC § 102

8. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Wagner et al

9. Claims 1-3, 12, 13 and 15-22 are rejected under **35 U.S.C. 102(b)** as being anticipated by Wagner et al (Helvetic Chimica Acta. Vol. 80: 200-212. 1997; cited in IDS filed on 9/22/04). The previous rejection is maintained for the reasons of record as set forth in the previous Office action. The rejection over 14 is moot due to applicant's cancellation of the said claims.

Discussion and Answer to Argument

10. Applicant's arguments have been fully considered but they are not persuasive for the following reasons (in addition to reasons of record). Each point of applicant's traversal is addressed below (applicant's arguments are in italic):

Applicants argue the Wagner reference does not teach all elements by stating the followings:

I. "Wagner neither teaches nor relies upon its potential fluorescent properties and does not indicate that the protecting group is detectable via any quantity of fluorescence that may be characteristic of this group.

II. "the Examiner offers no support for the contention that dnseoc either fluoresces or fluoresces to any extent detectable for purposes of the present methods."

III. "HPLC technology... not suitable for the on-chip or "on the array" analysis required by instant claim 1." (Reply, pp.8-9).

For applicant's first statement (I), the instant claims do not specifically recite a method of fluorescent detection. The instant claim 1 recites "carrying out a determination of the detectable

protecting groups", which recitation does not dictate that the "determination" step (step (c) of Claim 1) is a step of detecting the fluorescence of the protecting group.

In response to applicant's argument that the references fail to show certain features of applicant's invention, it is noted that the features upon which applicant relies (i.e., "*the protecting group is detectable via any quantity of fluorescence that may be characteristic of this group*") are not recited in the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993).

For Applicant's second statement (II), applicants seem to argue contrary to applicant's own disclosure and claims. As discussed in the previous office action, the protecting group "dnseoc" (or (dansyltheoxy)carbonyl) is a dansyl containing compound (ref., p.201; Figures). The instant claim 3 recites "the fluorescent groups are selected from the group consisting of compounds comprising pyrene, dansyl..." (emphasis added). Similarly, the instant specification also states "the detectable protecting groups are selected from fluorescent groups, e.g., groups comprising pyrene, dansyl..." (emphasis added; spec. p.6, [0022]). According to the instant disclosure, dansyl containing protection groups are fluorescent groups. Thus, the dnseoc groups of the Wagner reference read on the limitations of the instant claims.

For applicant's third statement, again, applicants have relied on features that are not recited in the instant claims. The instant claim (claim 1) language does not necessarily dictate that the signal detection step is carried out "on the array". The instant claim 1 recites the following steps:

"(b) cleaving off the detectable protecting groups, and

"(c) carrying out a determination of the detectable protecting groups on the array after cleavage"

The instant claim language can be broadly and reasonably interpreted to mean detecting (step (c)) those "protecting groups" that were presented "on the array" before (as in step (a)) but were cleaved off in step (b). That is the instant claim language does not necessarily limit the "determination" step is carried out "on the array". It is also not clear how the cleaved off protection groups can be specifically detected on the array.

Thus, the reference's teaching read on step (c) of the instant claim 1.

Applicants also state that the reference does not teach relying "on fluorescence of the cleaved protecting group or any differential fluorescence whatsoever". (Reply, p.9, para 2)

In response to applicant's argument that the references fail to show certain features of applicant's invention, it is noted that the features upon which applicant relies (i.e., *relying "on fluorescence of the cleaved protecting group or any differential fluorescence whatsoever"*) are not recited in the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993).

Applicants also state that the reference does not teach "Efficiency or completeness of deprotection using the detectable protection group to determine a degree of deprotection of the end product" and "quality control of on-array or on-chip synthesis with respect to complete deprotection". (Reply, p.9, para 3)

In response to applicant's argument that the references fail to show certain features of applicant's invention, it is noted that the features upon which applicant relies (i.e., "*Efficiency or completeness of deprotection using the detectable protection group to determine a degree of deprotection of the end product*" and "*quality control of on-array or on-chip synthesis with respect to complete deprotection*") are not recited in the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993).

Applicants also seem to argue that the Wagner reference is not enabled for "carrying out a determination of the detectable protecting groups on the array after cleavage" (Reply, p.9 para 4).

However, applicants have not provided any factual evidence to support the above assertion. As discussed above and in the previous Office action, the Wagner reference teaches every element of the claimed invention, and provides examples of making and using the described methods.

Claim Rejections - 35 USC § 103

11. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Wagner and Others

12. Claims 1-3, 12, 13 and 15-22 are rejected under **35 U.S.C. 103(a)** as being unpatentable over Wagner et al (Helvetic Chimica Acta. Vol. 80: 200-212. 1997; cited in IDS filed on 9/22/04), in view of Hobbs et al (5,151,507; 9/29/1992) and if necessary, Chen et al (Journal of Organic Chemistry. Vol. 66: 1725-1732; 2001). The previous rejection is maintained for the reasons of record as set forth in the previous Office action. The rejection over 14 is moot due to applicant's cancellation of the said claims.

Discussion and Answer to Argument

13. Applicant's arguments have been fully considered but they are not persuasive for the following reasons (in addition to reasons of record). Each point of applicant's traversal is addressed below (applicant's arguments are in italic):

Applicants traversed the above rejection with the same argument as the traversal over the Wagner reference alone. Thus, applicants are respectively directed to the discussion under the Wagner reference for answer to arguments.

Applicants, again, argue the Wagner reference does not teach "on the array" "determination of the detectable protecting groups". As discussed above, the feature "on the array determination" step is not specifically cited in the instant claims. The instant claim (claim 1) language does not necessarily dictate that the signal detection step is carried out "on the array". The instant claim 1 recites the following steps:

"(b) cleaving off the detectable protecting groups, and

"(c) carrying out a determination of the detectable protecting groups on the array after cleavage"

The instant claim language can be broadly and reasonably interpreted to mean detecting (step (c)) those "protecting groups" that were presented "on the array" before (as in step (a)) but were cleaved off in step (b). That is the instant claim language does not necessarily limit the "determination" step is carried out "on the array". It is also not clear how the cleaved off protection groups can be specifically detected on the array.

New Claim Rejections Necessitated by Amendment

Claim Rejections - 35 USC § 112

14. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

New Matter Rejection

15. Claim 22 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This rejection is necessitated by applicant's amendments to the claims.

Claim 22 has been amended to recite "wherein B is selected from the group consisting of adenine, guanine, cytosine, aza analogs thereof, deaza analogs thereof, and analogs thereof

containing additional amino groups" as filed on 10/2/07. The instant claim 22 as amended can be broadly and reasonably interpreted to mean analogs of "aza analogs", analogs of "deaza analogs", etc., which "analogs" of "analogs" do not appear to have support in the instant specification.

If Applicant believes this rejection is in error, applicant must disclose where in the specification support for the entire scope of the amendment(s) and/or new claims can be found. As a result, Claim 22 represents new matter.

Claim Rejections - 35 USC § 103

McGall and Others

16. Claims 1-3, 12, 13 and 15-22 are rejected under **35 U.S.C. 103(a)** as being unpatentable over McGall et al (US 6,238,862; 05/29/2001), Wagner et al (Helvetic Chimica Acta. Vol. 80: 200-212. 1997; cited in IDS filed on 9/22/04), in view of Hobbs et al (5,151,507; 9/29/1992) and if necessary, Chen et al (Journal of Organic Chemistry. Vol. 66: 1725-1732; 2001). This rejection is necessitated by applicant's amendments to the claims.

The instant claims recite a "quality control method for manufacturing a biopolymer array comprising (a) synthesizing a plurality of different biopolymer species on an array from monomeric or oligomeric building blocks comprising detectable protecting groups, (b) cleaving off the detectable protecting groups, and (c) carrying out a determination of the detectable protecting groups on the array after cleavage in order to determine the efficacy of deprotection,

wherein at least some of the detectable protecting groups couple to and protect nucleobase amino groups."

McGall et al, throughout the patent, teach methods of quality control for manufacturing nucleic acid probe arrays (e.g. Abstract and Claim 1 of the reference), which reads on the quality control method of **clm 1**.

The reference teaches synthesizing nucleic acids using protected monomers (e.g. Claims 5, 12 and 23; col. 2, lines 40+; Figure 9), which reads on step (a) of **clm 1** and nucleic acids of **clm 12**.

The reference teaches "deprotecting" (or removal) of the protecting group (e.g. Claim 23; col. 2, lines 40+; Figure 9), which reads on step (b) of **clm 1**.

The reference teaches "determining the amount of unprotected active sites" (col. 2, lines 49+) by detecting the amount of cleaved "detectable label" (col. 2, lines 55+), which reads on step (c) of **clm 1**.

The reference teaches the detectable label (or protecting label) is a fluorescent label such as a rhodamine (e.g. Claims 26 and 27 of the reference), which reads on the "fluorescent groups" of **clm 2** and rhodamine of **clm 3**.

The reference teaches the fluorescent label is linked (or coupled) to the nucleotide (e.g. Figure 6), which reads on the "coupled to nucleobases" of **clm 13**. The instant specification and/or claims do not specifically define the phrase "coupled to nucleobase". The phrase can be broadly interpreted to mean coupling the "protection group" (e.g. fluorescent label) and the "nucleobase" through any type of linkage (including both direct and indirect linkage). The

reference teaches linking the fluorescent label through the phosphate group in the sugar group of the nucleotide (e.g. Figure 6), and thus the label is "coupled" to the nucleobase of the nucleotide.

McGall et al do not explicitly teach the protection groups are coupled to and protect the nucleobase amino groups as recited in the amended **clm 1**. The reference also does not teach using "stilbene" (the elected species) as the "fluorescent group", as recited in **clm 3**. The reference also does not explicitly teach the various chemistries recited in **clms 15-22**.

However, **Wagner et al**, throughout the publication, teach methods of nucleic acid synthesis using protected nucleotides. (see Abstract). The reference teaches synthesis of various oligonucleotides using protected nucleotides (pp. 204-206; especially Table 1 and p. 204, last para). The reference teaches the fluorescent label is linked directly to the nucleobase (e.g. p. 202, Schemes 1-2), which reads on the "coupled to nucleobases" of **clm 13**, and coupling through the amino groups of **clm 1**.

The reference teaches the detectable label (or protecting label) is a fluorescent label such as a "dnseoc" (or a "dansyl") (e.g. p. 201, para 3 and Figures), which reads on the "fluorescent groups" of **clm 2** and "dansyl" of **clm 3**. The "dnseoc" ((dansylethoxy)carbonyl) group also reads on the "L" group when n=1 (as recited in **clm 21**), because the carbonyl group reads on the formula "C(O)" and the dansyl group reads on formula "R".

The reference also teaches the structure of nucleotides comprising a base (protected by dnseoc), a sugar, a protected hydroxyl group, and a protected phosphate group (e.g. Scheme 2, Scheme 5). The $(MeO)_2TrO$ (or Dimethoxytrityl) group in Scheme 5 of the reference (see p. 201, para 4 and p. 204) reads on the hydroxyl protection group, DMTrO (the elected species of ; see Reply, filed 3/6/07, p. 2) or the "triphenylmethyl" group of **clms 15, 16,** and **17**.

The reference also teaches phosphate protection group such as the "(2-cyanoethoxy)bis(diisopropylamino)phosphine" at the 3' sugar position (p. 204, para 1 and Scheme 5), which is the same phosphoramidite (phosphate amide) (i.e. the R3, R4, R5 and R6 groups of compound (f) in Figure 5 (the instant elected species; Reply, filed 3/6/07)), as recited in **clms 18, 19**, and **20**.

The reference also teaches various nucleobases such as C, A, and G (e.g. p. 204, Scheme 5), which read on the nucleotide bases recited in **clm 22** and the elected species of adenine.

Hobbs et al teach using various fluorescent molecules to label (or protect) nucleotides (see Abstract). The reference teaches "stilbene" can be used to attach to the nucleobases (col. 30, lines 20+) through linkers that comprise "carbonyl" group (reads on the formula of "COR" of **clm 21**; col. 11, lines 50+). The reference also teaches various fluorescent dye can be used depending on the different applications (cols. 12+).

In addition, **Chen et al**, teaches attaching "stilbene" to nucleosides (see Abstract). The Chen reference also teaches "stilbene" has "bright fluorescence of very high quantum yield" (p. 1725, right col., para 2).

Therefore, it would have been prima facie obvious for one of ordinary skill in the art at the time the invention was made to attach a fluorescent group such as "stilbene" to a "monomeric building block" (such as a nucleoside) to the amino groups of the nucleobase.

A person of ordinary skill in the art would have been motivated at the time of the invention to couple the protection group to the amino group of the nucleobase, because the nucleobase protection groups offer the advantages of providing more efficient and fast working oligodeoxyribonucleotide synthesis, as taught by Wagner et al (e.g. p.200).

A person of ordinary skill in the art would have been motivated at the time of the invention to use "stilbene" as the "detectable protecting group", because "stilbene" is a known fluorescent label for biomolecules (especially nucleotides), and stilbene is known to exhibit "bright blue fluorescence of very high quantum yield", as taught by both Hobbs et al and Chen et al.

A person of ordinary skill in the art would have been motivated at the time of the invention to use the specific nucleotide building blocks and their corresponding chemistry to generate the required reagent for the method of detecting deprotection, because the structures for basic nucleotide building blocks are known in the art, and the various protection groups are known and routine in the art as taught by Wagner et al. In addition, Wagner et al also teach the advantages of using these nucleotide building blocks and their corresponding protection groups, including providing efficient and fast working oligonucleotide synthesis as well as fast and effective cleavage of the protection group (e.g. pp.200-201).

A person of ordinary skill in the art would have reasonable expectation of success of achieving such modifications since McGall et al, Wagner et al, Hobbs et al and Chen et al have demonstrated successful attachment of various protection groups such as fluorescent groups (especially stilbene) to nucleosides through known reaction mechanisms (such as the formation of -HN-C=O linkage between the nucleobases and the stilbene molecule) as well as using various nucleotide building blocks to build oligonucleotides, as demonstrated by the said references.

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL.** See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sue Liu whose telephone number is 571-272-5539. The examiner can normally be reached on M-F 9am-3pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Doug Schultz can be reached at 571-272-0763. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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Art Unit 1639
11/2/2007

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